REMARKS

Claims 3-12 and 14-17 are pending in this application. Claims 3-12 and 14-17 are rejected. In view of the following remarks, reconsideration of claims 3-12 and 14-17 is respectfully requested.

Claim Rejections - 35 USC § 103

Claims 3-12 and 14-17 have been rejected under 35 U.S.C. 103(a), as being obvious over Hiserodt *et al.* (US patent No. 6,277,368) and in view of Ferrante *et al.* (Cancer Chemother. Pharmacol., 43(Suppl.): S61-S68, 1999).

Hiserodt *et al.* is directed to the use of a vaccine in cancer immunotherapy. As mentioned in the abstract of Hiserodt *et al.*, the disclosed vaccines only comprise a source of tumor-associated antigen and a cytokine-secreting cell-line. Although Hiserodt *et al.* recite that the Hiserodt compositions may be given following, preceding, in lieu of, or in combination with, other cancers therapies (e.g. radiation therapy, chemotherapy) (see paragraph 140 of Hiserodt *et al.*), the only time Hiserodt *et al.* uses **a combination therapy** that involves administering a chemotherapeutic agent and a vaccine containing tumor cells to cancer patients is in Example 7 where the chemotherapeutic agent Cisplatin is administered to the ovarian cancer patients nine days after they have received the last injection of the Hiserodt *et al.* vaccine. Thus, as acknowledged by the Examiner (see paragraph 7 of the Office Action), Hiserodt *et al.* does not teach a single composition that contains tumor cells, chemotherapeutic agent, and carrier, as recited in claim 3 of the instant application. Moreover, Hiserodt *et al.* cautions that radiation therapy and adjuvant chemotherapy be used 'in a way or at a time that does not interfere with the immunogenicity of the Hiserodt compositions' (see paragraph 140 of Hiserodt *et al.*). Thus, it is reminded to the Examiner that Hiserodt *et al.* suggests that there is ***considerable unpredictability in the art of anti-cancer immunogenic compositions***. In other words, one of ordinary skill in the art, upon reading Hiserodt *et al.* as a whole would not have believed that adding an adjuvant therapy, the immune system of the patient would have been impaired, causing interference and thus reducing the efficiency, hence the dissociation in time over nine days of both treatments. Thus one skilled in the art would not reasonably believe that the immunogenic composition recited in claim 3 of the instant application would be efficacious, much less that adding a

chemotherapeutic agent to tumor cells would greatly enhance the immunogenicity of such a composition as shown in Examples III and IV of the instant application.

Furthermore, Ferrante *et al.* does not provide the teachings and suggestions absent from Hiserodt *et al.* Ferrante *et al.* is not directed at enhancing the immunogenicity of compositions that contain inactivated tumor cells. Instead, Ferrante is directed to a brief overview of the chemotherapeutic effects of Paclitaxel, Cisplatin and doxorubicin. Again, this reference is only teaching the sequential addition of Paclitaxel to standard adjuvant therapy with doxorubicin and cyclosphosphamide (see pS62 in Ferrante). Moreover, unlike the immunogenic compositions of the instant claims, which comprise tumor cells and chemotherapeutic agents, the compositions disclosed in Ferrante *et al.* also only contains two chemotherapeutic agents such as cisplatin and Paclitaxel (see p.S62 in Ferrante). Thus, nowhere is it taught in Ferrante an anti-cancer composition comprising an 1) antigen, 2) at least one immunomodulator chemotherapeutic compound and 3) a pharmaceutically acceptable carrier, the composition eliciting an immune response in a patient wherein the antigen is inactivated tumor cells from a cancer targeted by the composition. Accordingly, upon reading both Hiserodt *et al.* and Ferrante *et al.*, the skilled artisan still would not reasonably expect that that the immunogenic composition recited in claim 3 of the instant application would be efficacious, much less that adding a chemotherapeutic agent to a composition containing tumor cells would greatly enhance the immunogenicity of such a composition.

The composition described in the present patent application identified hereinabove teaches the use of such composition in a "monotherapy", meaning allowing treating a patient with only one drug. More specifically, claim 3 is directed to an anti-cancer composition comprising an 1) antigen, 2) at least one immunomodulator chemotherapeutic compound and 3) a pharmaceutically acceptable carrier, the composition eliciting an immune response in a patient wherein the antigen is inactivated tumor cells from a cancer targeted by the anti-cancer composition. Monotherapy present important advantages for the patient such as lower treatment costs, simpler dosing schedule and simplifying the monitoring of adverse effects. One surprising element of the present invention, which is well explained on page 9 of the description of the present application, is that it is possible to enhance immunogenecity of a composition, such as a vaccine for example, by combining directly the chemotherapeutic agents with the vaccine in one

single administration. Thus, the composition described in the present application stimulates an immune response and provides an anti-tumor effect against cancer cells as demonstrated in Examples III and V. Secondly, the composition of the present application is unique in that the composition comprises two specific elements consisting of an antigen consisting of inactivated tumor cells from a targeted cancer and a chemotherapeutic agent.

In view of the above, it is believed that claims 3-12 and 14-17 are inventive over Hiserodt *et al.* and in view of Ferrante *et al.*, taken alone or in combination.

Claims 3-12 and 14-17 are rejected under 35 U.S.C. 103(a), as being obvious over Wang *et al.* (Cancer Immunol., 1986) and in view of Ferrante *et al.* (Cancer Chemother. Pharmacol., 43(Suppl.): S61-S68, 1999).

It is resubmitted to the Examiner's attention that Wang *et al.* only teaches the administration of CL 259,763 to animals by gavage (see page 8, second column, fourth paragraph of Wang *et al.*). Further, it is clearly indicated in Wang *et al.* (page 10, first column, third paragraph) that the mice were vaccinated with L1210 tumor cell and subsequently given test compound by gavage. Thus, the combination therapy of Wang *et al.* is comparable to the combination therapy of Hiserodt *et al.* except that the test compound was given in a **different way** as well as a **different time** as the tumor cells. Accordingly, Wang *et al.* is even less likely to motivate one of ordinary skill in the art to add a chemotherapeutic compound to a composition that comprises tumor cells. Further, as mentioned hereinabove, Ferrante is only directed to the chemotherapeutic effects of Paclitaxel, Cisplatin and doxorubicin. Ferrante is only teaching the sequential addition of Paclitaxel to standard adjuvant therapy with doxorubicin and cyclosphosphamide (see pS62 in Ferrante). Moreover, unlike the immunogenic compositions of the instant claims, which comprise tumor cells and chemotherapeutic agents, the compositions disclosed in Ferrante *et al.* also only contains two chemotherapeutic agents such as Cisplatin and Paclitaxel (see p.S62 in Ferrante). Thus, Ferrante *et al.*, cannot lead a person skilled in the art to the preparation of a composition allowing a monotherapy **efficient** in stimulating immune response and antitumor response against cancer cells. Again, none of the references cited by the Examiner have demonstrated or even suggested, even when considered together, the observed superior effect of

a composition comprising an antigen consisting of inactivated tumor cells from a cancer targeted by the composition and a chemotherapeutic compound.

In view of the above, it is believed that claims 3-12 and 14-17 are inventive over Wang *et al.* and in view of Ferrante *et al.*, taken alone or in combination.

It is submitted therefore that the claims are in condition for allowance. Reconsideration of the Examiner's rejections are respectfully requested. Allowance of claims 3-12 and 14-17 at an early date is solicited.

In the event that there are any questions concerning this response, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedite

Respectfully submitted,

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